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ANESTHESIA AND RESUSCITATION

Hyperbaric Oxygen Therapy and Sepsis.

Advantages and Limits

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Sepsis and its sequelae are the leading causes of mortality in intensive care units, accounting for 10% to 50% of the deaths in ICUs.

Release of endotoxin from cell wall, in fact, is believed to initiate the signs, symptoms, and biochemical abnormalities that characterise septic shock.

The concert of cytokines represents one of the crucial events of inflammatory reactions but there are several others with various metabolic consequences always leading to tissue damage and multiorganic deficiences as: cythokins and interleukins, which are tumours necrosis factor (TNF); the complement system: the extrinsic coagulation pathway and the fibrinolytic system; cell components like neutrophils, monocytes, endothelial cells and blood platelets. TNF, which is released by mononucleates, is a base-mediator able to release other cytokins (IL-1, IL-6, IL-8); TNF activates either endothelial cells or endothelins, neutrophils and some coagulative processes; hemodynamic, cardio-ventricular functions, pulmonary and intestinal permeability take place, and these are peculiar to sepsis.

Many clinico-experimental data showing that tissue hypoxia, at least experimentally, doubles the plasmatic half-life of toxins and drugs with respect to normal oxygen level in rats. In fact, experimental studies with toxic substances or drugs on hypoxic rats, lead us to assume consequences, prolong the permanences in the circulus of exotoxins and mediators of sepsis, with reduction in kidney hematic flow and gromerular filtration.

The interaction between oxygen and antimicrobial agents have important implication for the therapy of infections, because oxygen tensions can profoundly affect the static activity of certain antimicrobial agents against specific microorganisms (1).

Increased oxygen tension can induce changes in host tissues (e.g., decreased reduction-oxidation potential and increased pH) that may influence the metabolism and/or activation of certain antimicrobial agents. Increased oxygen tensions can also induce metabolic or genetic responses in microorganism (e.g., increased trasmembrane potential, decreased protein biosynthesis, induction of antioxidant defenses) that alter the susceptibility of the microorganism to antimicrobial agents.

Oxygen tensions profundly influence the activity of aminoglycosides by at least two mechanism. The first mechanism of action of oxygen involves the uptake of the aminoglycosides into the bacteria. Uptake begins with diffusion of the aminoglycoside through the cell wall into the periplasmic space of Gram negative bacteria. The antimicrobial is then transported into the cell cytoplasm by low affinity carrier(s) in thebacterial cytoplasmic membrane. This transport is oxygen - and energy-dependent.

The antimicrobial activity of fluorquinolones is due to the inhibition of the critical bacterial enzyme DNA gyrase.

Fluorquinolones have a broad spectrum of activity against both Gram-positive and Gram-negative aerobic bacteria. Activity against anaerobes is limited. In addition, it appears that an aerobic environment is required for antimicrobial activity. Interestingly, low pH may also inhibit the activity of some of the fluorquinolones. These considerations have led to the recommendation that fluorquinolones should not be employed in infected tissues in which low oxygen tensions are likely to prevail; examples are osteomielitis and infections involving protheses.

The beneficial effects of adjunctive hyperbaric oxygen for the treatment of bacterial infections have been demonstrated in a few animal models.

The potentiation of the activity of antimicrobial agents by oxygen was recently studied in a rat model of polymicrobial sepsis induced by cecal ligation and puncture. The rat model is very reproducible and lenght of survival, and mortality were used as measures to assess the effects of hyperbaric oxygen therapy.

Hyperbaric oxygen also appeard to potentiate the activity of vancomycin and clindamycin, but not metronidazole in the sepsis model (2). The effect of vancomycin are in agreement with the results from in vitro work discussed previously. The effect of metronidazole are similar to those obtained with the septic model discussed previously and are at variance with data from in vitro work. Our last work demostred that H.B.O.T. had significant influence on bacterial infection by P. Aeruginosa (3).

The P. Aeruginosa is a Gram-negative bacterium pertaining to the Pseudomonadaceae family. It is responsable for 6-22% of all hospital infections.

In rats affected by P. Aeruginosa, H.B.O.-induces a significant reduction in mortality and morbility with

bacteria eradication in blood culture findings, bronchial aspirate and skin biopsies. These effects were increased by the use of amikacine which is an antibiotic used for the treatment of Gram-negative bacteria.

Consideration of the mechanisms of action of oxygen on the activity of antimicrobial agents in vitro and in vivo indicates that oxygen tensions are an important determinant of the activity of certain antimicrobial agents. Hence, restoration of oxygen tension in hypoxic-infected tissue to normal by various means, including hyperbaric oxygenation, is an important therapeutic goal.

Some of the mechanisms of action of oxygen will require further elucidation, but it is clear that hyperbaric oxygen can play an importan role in the control of growth of certain bacteria during the cellulo-molecular responses in sepsis.

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